Estimating Illicit Drug Consumption Rate Through Wastewater-Based Epidemiology: A Survey On Selected Communities In Southeastern Brazil

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Abstract:

Background: Estimating illicit drug use on a community level by wastewater-based epidemiology (WBE) is both an objective and reliable way to establish near-real-time results. With high productivity, convenience, objectivity, and semi-real-time benefits, WBE has been demonstrated to be a powerful tool. It has been utilized on a global scale for monitoring illicit drug use.

Materials and Methods: For five consecutive days, wastewater samples were collected from eight wastewater treatment plants and analyzed for [amphetamine (AMP), methamphetamine (METH), 3,4-methylenedioxymethamphetamine (MDMA), cannabis and cocaine]. Drug consumption estimation based on WBE requires sewage sampling strategies that express concentration along the whole period. To this end, the most common approach is the use of automatic composite samplers.

Results: Seven out of the 11 targeted drug residues had 73.5% detection frequency (percentage of the samples containing drug residue >limit of quantification or not detected) in the wastewater influents.

Conclusion: With the increase in drug consumption in recent decades, in particular cocaine and cannabis, the social impact on society has also propagated. These consequences include rising healthcare costs, crime rates, and economic losses. Therefore, policymakers must gain knowledge of the trends, usage levels, hot spots, and the overall prevalence of illicit drug consumption, to develop proper prevention campaigns and effective intervention strategies.

Key Word: Illicit drugs; Wastewater-based epidemiology; Psychotropic substance; Drug use.

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I. Introduction

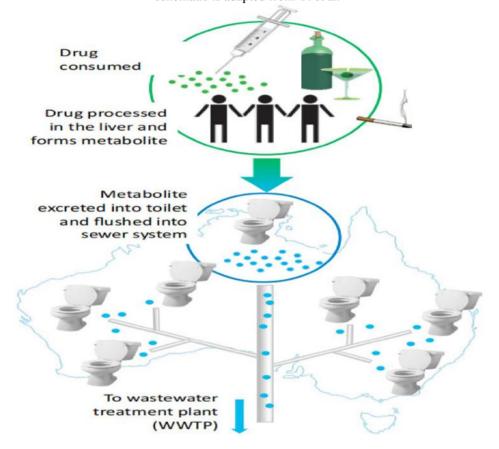
Illicit drug use has been long debated and plagued society, especially in the modern world with new drugs surfacing rapidly. While some argue the beneficial and medicinal effects of some drugs, particularly cannabis typically¹, illicit drug use harms society, and is viewed as being responsible for immense social, medical, policing, and economic burdens². Illicit drug use in the community has been shown to affect the individual's interaction and connection to society, often resulting in detrimental disconnection from the world around them. Drug use not only affects the user but also their family and friends, extending out to the community around them³.

According to Delker et al.⁴, estimation of drug use at the population level is traditionally performed via socio-epidemiological methods, such as population surveys. These data are subject to significant uncertainties in measurement and selection, for example, self-reporting bias from false reports, unaware or misinformed consumers, and limited population coverage of the study.

As shown in Figure 1. Wastewater-based epidemiology (WBE) consists in acquiring relevant information about the lifestyle and health status of the population through the analysis of wastewater samples collected at the influent of a wastewater treatment plant⁵. Additionally, WBE can provide information on the risk factors and health status of a population through analysis of their wastewater³. The advantage of this tool over classical epidemiological techniques (retrospective data analysis, surveys, and/or direct monitoring of many individuals) is that it achieves rapid (almost real time) data collection, which makes WBE an early warning tool. In addition, these data represent a pool of the global population or at least an important percentage of it. The potential of wastewater to serve as a reflection of the substances consumed or to which the population is exposed was predicted by Daughton⁶ who already described wastewater as an instrument that through the

measurement of chemical compounds and metabolites (biomarkers in a global way) would evaluate the population's health.

Figure 1. Schematic illustrating the course of drug transportation, starting from the ingestion of chemicals to the production of metabolized waste products that are eventually discharged into the sewer system. This schematic is adapted from Yi et al.⁷



Analysis of wastewater for indicators of illicit drug use was one of the first proposed applications of WBE⁶. It has been successfully applied to estimate illicit drug consumption and is based on the chemical analysis of specific drug metabolites in raw wastewater as indicators of the ingestion of the parent drug⁸. This approach has enormous potential to complement current epidemiological methods in view of the objective, up-to-date results, and it can, therefore, be extended to a wider range of substances⁶.

Thus, measuring target drug metabolic residues in raw wastewater allows the identification of the use of specific substances by a population. In WBE, the residual level of drug biomarkers in raw wastewater is used to retroactively calculate community drug consumption, which can reveal trends and subsidize public health policies^{9,10}. According to EMCDDA¹¹, the method consists of several consecutive steps that allow researchers to identify and quantify target metabolic residues of illicit drugs in raw wastewater and back-calculate the amount of the corresponding illicit drugs that would have been consumed by the population served by the wastewater treatment plant (WWTP). After entering the sewer network, these excreted agents arrive at WWTP where wastewater samples can be collected over a defined sampling period.

The prevalence of drug use and dependence is growing as a global threat to social and economic wellbeing². Traditionally, the incidence of drug use has been valued based on a combination of toxicology reports, self-reported survey questionnaires, and crime statistics. Conservative approaches suffer from excessive cost, limited coverage, generating delays for the immediate need for intervention, including non-response bias in the selection of the sample from the population with the highest drug use; therefore, potentially underestimating actual drug use¹². In Brazil, the illicit drug epidemic continues to prevail, with the key factor being the increase in deaths related to drug use, which is associated with thousands of tragedies and family miseries. The cost of social capital, directly or indirectly related to the production, trafficking, and consumption of illicit drugs, is also enormous¹³. Indeed, timely, cost-effective, and comprehensive measurement of substance use prevalence has never been more imperative before. The impact of illicit drug use on society can be classed into two types: tangible and intangible costs4. Tangible costs are the quantifiable costs to society, which can be categorized as those resulting from (1) workplace labour, (2) labour in the household, (3) healthcare and (4) crime. Examples of the quantifiable costs because of illicit drug use from each category are briefly elaborated; (1) reduction in the workforce and absenteeism, (2) premature death and illnesses, (3) pharmaceuticals, hospital, and medical costs, and (4) policing, courts and prison¹⁴.

The literature contains two important documents, albeit with regional data: *i*) The 'Social Costs of Cannabis Use to Australia' report was published in June 2020 and reported on costs incurred in the 2015/16 financial year. Overall, the cost of cannabis use was estimated at \$4.5 billion: \$4.4 billion in direct tangible costs, including through crime and criminal justice, hospital and other health care costs, reduced productivity and worker absence, and road traffic crashes; and *ii*) The criminal justice system accounted for more than half of all tangible costs. A further \$100 million was estimated for intangible costs due to premature death, mostly through cannabis-related road traffic crashes, resulting in more than 850 years of life lost¹⁴. The Social Costs of Methamphetamine in Australia report was published in July 2016 and relates to costs incurred in 2013/14. The overall cost was \$5.0 billion, with 170 deaths attributed to methamphetamine. These deaths were responsible for \$12 million through tangible costs arose in the criminal justice domain (\$3.2 billion), followed by workplace costs (\$289 million), child maltreatment/protection (\$260 million) and healthcare (\$200 million)¹⁵.

The purpose of measuring societal drug use is to understand the true social use of drugs. With the ability to accurately assess social drug use in real-time, the efforts of various community groups, such as law enforcement, government agencies, medical professionals, and policy agencies, can be better targeted and budgeted. Drug use has a significant impact on all facets of a community. Millions of individuals have been reported to be current users of illicit drugs such as cocaine, heroin, amphetamine, and methamphetamine². The consequences of using these drugs have a negative ripple effect on the rest of the community. From causing significant negative consequences on individual health to decreasing social behavior, extending its impact to family and friends and the rest of the community¹⁶. The impact of illicit drug use is devastating, with some individuals developing substance abuse disorders and dependence¹⁷. According to Ferreira et al.¹⁸ estimating social drug use in society allows the best strategies to be formulated to combat it.

Study area

II. Material And Methods

The State of Rio de Janeiro is one of the twenty-seven federative units of Brazil. It occupies an area of 43,780,172 km². It is composed of ninety-two municipalities, which are distributed in eight government regions of the State of Rio de Janeiro (Latitude 23°0'1.3392" S, Longitude: 43°21'57.2184" W). It is in the southeast of the country's Southeast region, bordering the State of Minas Gerais (north and northwest), State of Espírito Santo (northeast) and State of São Paulo (southwest), in addition to the Atlantic Ocean (east and south)¹⁹.

Chemicals and materials

Standard solutions of cocaine (COC), benzoylecgonine (BZE), norcocaine (NOR), ecgonine methyl ester (EME), cocaethylene (CET), 3,4-methylene-dioxy-N-methylamphetamine (MDMA), 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxy-Nethylamphetamine (MDEA), methamphetamine (MET), amphetamine (AMP), 11-nor-delta-9-hydroxytetrahydrocannabinol (THC-COOH), cocaine-d₃, BZE-d₃, EME-d₃, CET-d₈, MDMA-d₅, MDA-d₅, MDEA-d₅, MET-d₅, AMP-d₆, THC-COOHd₃, in methanol (MeOH) or acetonitrile (ACN), were purchased from LGC Standards (São Paulo, Brazil). MeOH and ACN, HPLC grade (Hipersolv Chromanorm), formic acid (FA) (Normapur) and ammonium formate (AF) (Normapur) were purchased from VWR (São Paulo, Brazil) (Scharlab Brazil S/A). Ultra-pure water was produced using successive Milli-RO reverse-osmosis filtration and the Milli-Q Plus water purification system (Merck Millipore, Rio de Janeiro, Brazil).

Solid Phase Extraction (SPE) cartridges Oasis HLB (500mg/6mL) and Xbridge Phenyl 3.5mm, 3 mm×150mm HPLC column were purchased from Merck (Rio de Janeiro, Brazil). The instrumental analysis was performed with a Thermo Scientific® LC system equipped with a pump (Accela 600 pump) and an autosampler coupled with a triple quadrupole mass spectrometer (Thermo Scientific TSQ Quantum Access Max, Thermo ScientificTM, Belo Horizonte, Brazil), operated in the electrospray negative ionization mode.

Sampling location and sample collection

For this research were selected the Municipalities: Resende (Latitude: 22°27'45.55"S and Longitude: 44°27'19.99"W), Petropolis (Latitude: 22°30'16.70"S and Longitude: 43°10'56.38"W), Niteroi (Latitude: 22°52'50.75"S and Longitude: 43°6'15.61"W), Rio de Janeiro (Latitude: 22°54'29.9988" S and Longitude:

43°11'46.9968" W), Cabo Frio (Latitude: 22°52'43.26"S and Longitude: 42°1'11.55"W), Nova Friburgo (Latitude: 22°17'13.69"S and Longitude: 42°32'1.31"W), and Campos dos Goytacazes (Latitude: 21°45'16.08"S and Longitude: 41°19'27.87"W). Aspects of the selected WWTPs are summarized in Table 1.

able 1. Characteristics of the investigated wastewater freatment frants (www.fr				
Municipality	WWTP	Population assisted		
Cabo Frio	Cabo Frio	222,528		
Niterói	Icaraí	75,700		
Petrópolis	Quitandinha	70,000		
Rio de Janeiro	Ilha do Governador	250,000		
	Pavuna	120,000		
	Barra da Tijuca	394,037		
Nova Friburgo	Centro	38,461		
Campos dos Goytacazes	Esplanada	202,000		

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able 1.	Characteristics of the	e investigated	wastewater	Treatment Plants ((WWIP)

The samples were collected from eight WWTPs varying in catchment size (38,461-394,037 inhabitants) and type of treatment technology, which were choice to have representative capacities, Rio de Janeiro locations and types of treatment. We selected the WWTPs in three capacity groups of Equivalent Inhabitants (EI): big with EI>200,000 EI, medium with EI ranging from 50,000 to 150,000 EI and small with EI ranging from 10,000 to 40,000 EI.

Every WWTP provided aliquots of composite samples from the influent, representing raw wastewater over a 24-hour period. Typically, samples were obtained for five consecutive days (july 2024). At the end of sampling, 5L samples were collected in polypropylene bottles and sent to laboratory in a cool box intended to be used for 24h shipments. Upon receipt, samples were filtered and extracted according to the following protocol and the extracts were stored at 4°C before analysis²⁰.

Related to compounds of interest, the human metabolic residues were targeted in wastewater (influents) as shown in Table 2.

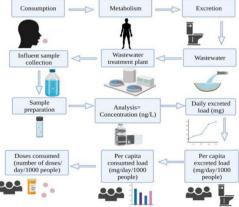
Drug	Compound of interest	Abbreviation
Cannabis	11-Nor-9-carboxy- Δ^9 -tetrahydrocannabinol	THC-COOH
	Cocaine	COC
	Benzoylecgonine	BE
Cocaine	Cocaethylene	COE
	Ecgonine methyl ester	EME
	Norcocaine	NCOC
Amphetamine	Amphetamine	AMP
Methamphetamine	Methamphetamine	MAMP
Ecstasy	3,4-Methylenedioxymethamphetamine	MDMA
	3,4-methylene-dioxy-N-methylamphetamine	MDHMA
	3,4-methylenedioxyamphetamine	MDA

Table 2. Compounds of interest	(human metabolic residues)
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Drug consumption

Consistent with the scheme presented in Figure 2, the workflow in wastewater-based epidemiology model is an important tool for monitoring patterns and trends in illicit drug consumption in communities, by detecting drugs, making it possible to monitor habits and lifestyle, as well as associated outcomes in health, education and crime²¹.

Figure 2. Scheme of the workflow in Wastewater-Based Epidemiology (WBE) adapted from Gerber et al.²¹



The estimated illicit drug use was normalised to the number of inhabitants served by the WWTPs. The excretion rates of the selected drugs were used to calculate the drug concentrations normalised per 1000 inhabitants as well as 1000 inhabitants in the age group of 15-64 years (69.1% of the total population). The estimates of the fraction of the drugs excreted in urine was used to obtain a consumption value for each drug within the community²²⁻²⁴.

For the back calculations, concentrations (ng/L) of the drugs or metabolites in WWTP influents, daily flow rate (L/day) of the WWTP influent and the correction factors are used. The back-calculation equations used for cocaine (equation 1), amphetamine (equation 2), methamphetamine (equation 3), MDMA (equation 4), and THC (equation 5) as follows:

Cocaine $(g/day) = concentration of benzoylecgonine (ng/L) * flow rate (L/day) * 2.33$	equation (1)
Amphetamine $(g/day) = concentration of amphetamine (ng/L) * flow rate (L/day) * 3.3$	equation (2)
Methamphetamine (g/day) = concentration of methamphetamine (ng/L) * flow rate (L/day) *	2.3 equation (3)
MDMA (ecstasy) (g/day) = concentration of $MDMA$ (ng/L) * flow rate (L/day) * 1.5	equation (4)
THC (cannabis) (g/day) = concentration of THC-COOH (ng/L) * flow rate (L/day) * 10	equation (5)

Total amount of each drug (mg/day *per* 1000 inhabitants) was back-calculated using the concentration of the parent drug and/or metabolite in influent wastewater and the daily flow rate of the parent drug and/or metabolite in the WWTPs. The knowledge of several parameters is essential: (I) consumption indicators, (II) excretion rates, (III) correction factors and, (IV) average drug dose (Table 3).

Illicit drug	Illicit drug target residue	Illicit drug excretion dose as target residue	Correctio n factor	Dose (mg)
Amphetamine	Amphetamine	30 ^(e)	3.3 ^(e)	30 ^(e)
Cocaine	Benzoylecgonine/Coc aethylene	45 ^(e)	2.33 ^(c)	100 ^(d)
MDMA (ecstasy)	MDMA	65 ^(e)	1.5 ^(e)	100 ^(d)
Methamphetamine	Methamphetamine	43 ^(e)	2.3 ^(e)	50 ^(e)
THC (cannabis)	THC-COOH	$0.6^{(e)}$	10 ^(b)	125 ^(a)

Table 3. Parameters used in the back-calculation process of each illicit drug

^(a)Postigo et al.²⁵, ^(b)van Wel et al.²⁴, ^(c)Zuccato et al.²², ^(d)Terzic et al.²⁶, ^(e)van Nuijs et al.²⁷

Analytical methods: Solid Phase Extraction

All chemical analyses were performed by *Laboratorio de Técnicas Espectroscópicas* (LABTE), Rey Juan Carlos University, Madrid, Spain. Analytical methodologies were based according to Hernández *et al.* (2018), which generally consisted of: (*i*) spiking samples with stable isotope-labelled internal standards (SILIS) for each analyte, in order to correct for matrix interferences and/or losses during sample treatment; (*ii*) filtration or centrifugation of samples to remove solid particles; (*iii*) off-line solid-phase extraction (SPE) for preconcentration and clean-up; and (*iv*) analysis by liquid chromatography coupled to tandem mass spectrometry (LC-MS-MS). Samples were filtered on glass fiber filters (1mm, GF/B Whatman) before SPE extraction. Isotopically labelled compounds were added to 250mL of WWTP influent (250µL of a 200µg/L methanolic solution of each deuterated compound). Cartridges were conditioned by following elution of 2×5mL MeOH and 2×5mL ultra-pure water. Samples were percolated at a flow rate of 2mL/min. The SPE cartridges were then washed using 2×5mL ultra-pure water and dried for 30 min. Analytes were eluted with 2×5mL of MeOH and eluates were evaporated to dryness under a gentle stream of nitrogen. Extracts were reconstituted in 500mL of MeOH and kept frozen until analysis. A 5µL volume was injected for LC-MS-MS analysis.

Liquid chromatography tandem mass spectrometry (LC-MS-MS) measurement

LC-tandem MS (LC-MS-MS) coupled with electrospray ionization was used for sample analysis. LC separation was performed with a Waters 2695 high-performance LC separation module (Milford, MA, USA), and MS-MS analyses were performed using a Micromass Quattro triple-quadrupole mass spectrometer (Micromass, Manchester, UK). MS data acquisition and analysis was performed using MassLynx Version 4.0 software (Micromass, Manchester, UK).

GC–MS was performed on a Varian CP-3800 GC equipped with Varian Chrompak Saturn 2000 GC– MS and Varian CP-8400 autosampler (Palo Alto, CA). The column was Rxi-XLB ($30mL \times 0.25mm$ ID $\times 0.25$ µm film thickness) from Restek (Bellefonte, PA). The oven temperature program was held at 60°C for 5 min, programmed at 30°C/min to 190°C and held for 9, followed by 20°C/min to 250°C and held for 3.67 min ²⁸. The injector temperature was 260°C. The MS was operated in the full scan mode, 150-500 m/z mass range, under positive-ion electron impact conditions.

Statistical Analysis

Data analysis (counts, percentages, and means) were performed with Excel software (Microsoft 365®). All statistical analyses were performed using Jamovi (Version 2.5). Statistically significant differences of the median were judged by one-way analysis of variance (ANOVA) and least significant differences calculations at a 5% significant level.

Research Ethics Committee

This research was approved by the Research Ethics Committee, Sergio Arouca National School of Public Health/Oswaldo Cruz Foundation, Protocol 07/2018.

III. Result

Occurrence of illicit drugs and metabolites in the influent WWTPs

The average occurrence of AMP – amphetamine; MAMP – methamphetamine; MDMA – 3,4methylenedioxymethamphetamine; COC – cocaine; COE - cocaethylene; BE – benzoylecgonine; THC-COOH – 11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol in the wastewater (in ng/L) of each city are presented in Table 4.

 Table 4. Concentration (average ± standard deviation) of biomarkers (ng/L) in sewage samples collected in thirteen WWTPs of the Hydrographic Region, Rio de Janeiro State

		Biomarker						
WWTP	HRRJ	AMP	МАМР	MDMA	COC	BE	COE	THC- COOH
				Averag	e ± standard dev	iation (ng/L)		
Quitandinha	Petrópolis	nd	nd	nd	1659 ± 61	1955 ± 47	nd	244 ± 21
Icaraí	Niterói	165 ± 8	133 ± 7	151 ± 8	2433 ± 77	$\begin{array}{c} 26775 \pm \\ 66 \end{array}$	nd	412 ± 14
Ilha do Governador		322 ± 12	<loq< td=""><td>288 ± 11</td><td>2544 ± 59</td><td>3451 ± 79</td><td>241 ± 18</td><td>477 ± 16</td></loq<>	288 ± 11	2544 ± 59	3451 ± 79	241 ± 18	477 ± 16
Pavuna	Rio de Janeiro	166 ± 13	145 ± 5	544 ± 16	3988 ± 122	4316 ± 56	271 ± 13	555 ± 14
Barra da Tijuca		397±8	313 ± 11	581 ± 13	3155 ± 83	3777 ± 49	276 ± 19	688 ± 23
Cabo Frio	Cabo Frio	399 ± 11	<loq< td=""><td>533 ± 12</td><td>3320 ± 83</td><td>4111 ± 53</td><td>344 ± 37</td><td>456 ± 23</td></loq<>	533 ± 12	3320 ± 83	4111 ± 53	344 ± 37	456 ± 23
Centro	Nova Friburgo	<loq< td=""><td><loq< td=""><td><loq< td=""><td>1944 ± 56</td><td>2265 ± 47</td><td>166 ± 15</td><td>224 ± 19</td></loq<></td></loq<></td></loq<>	<loq< td=""><td><loq< td=""><td>1944 ± 56</td><td>2265 ± 47</td><td>166 ± 15</td><td>224 ± 19</td></loq<></td></loq<>	<loq< td=""><td>1944 ± 56</td><td>2265 ± 47</td><td>166 ± 15</td><td>224 ± 19</td></loq<>	1944 ± 56	2265 ± 47	166 ± 15	224 ± 19
Esplanada	Campos dos Goytacazes	nd	nd	nd	562 ± 43	<loq< td=""><td>nd</td><td>276 ± 32</td></loq<>	nd	276 ± 32

Abbreviations: HRRJ - Hydrographic Region - State of Rio de Janeiro; WWTP - Wastewater Treatment Plant; AMP – amphetamine; MAMP – methamphetamine; MDMA – 3,4-methylenedioxymethamphetamine; COC –

 $cocaine; COE - cocaethylene; BE - benzoylecgonine; THC-COOH - 11 - nor - 9 - carboxy - \Delta^9 - carboxy - 20 - carboxy -$

 $tetrahydrocannabinol; \ LOQ-limit \ of \ quantification; \ (<) \ below \ LOQ; \ nd-not \ detected.$

Seven out of the 11 targeted drug residues had 73.5% detection frequency (percentage of the samples containing drug residue >limit of quantification or not detected) in the influent WWTPs. Quantities of drug residues in wastewater influents are, among others (e.g., excretion rate), closely related to the level of drug use found by Deng et al.²⁰. The sample from Pavuna showed the highest mean concentration in influent for cocaine (3988 ng/L), Cabo Frio for cocaethylene (344 ng/L), and Bara da Tijuca for methamphetamine (313 ng/L). Cabo Frio showed the highest mean concentration in influent for amphetamine (399 ng/L), and Ecstasy (581 ng/L), Pavuna for benzoylecgonine (4316 ng/L); and Barra da Tijuca showed the highest mean concentration in influent for *cannabis* metabolite (THC-COOH) (688 ng/L).

Drug consumption values

The estimation was performed only for 5 illicit drugs, including cocaine, amphetamine, MDMA (ecstasy), and THC (marijuana) are presented in Table 5. The WWTPs researched were those that had the highest concentration of illicit drugs, such as: Icaraí, Ilha do Governador, Pavuna, Barra da Tijuca, and Cabo Frio. The applied methodology considers the known metabolic pathways of selected drugs, the molar ratio of

metabolite to parent drug as well as the percentage of a selected drug target residues, excreted after consumption of the parent drug. They were performed in accordance with the guidelines proposed by Zuccato et al. ²⁹, Postigo et al. ²⁵, Terzic et al. ²⁶, van Nuijs et al. ²⁷, and van Wel et al. ²⁴.

The representative excretion rates of the selected drug target residues were applied to calculate the drug abuse normalised on 1000 inhabitants as well as on 1000 inhabitants in the age group of 15-64 years. The correction factors to convert excreted amounts of individual drugs into consumed amounts were taken from the literature and are briefly summarized in Table 4. The estimated total consumption was normalised to the number of citizens served by investigated WWTPs (mg/day/1000 inhabitants).

	Illicit drug (metabolite)				
WWTP	AMP	MDMA	COC	тнс-соон	
mg/day/1000 inhabitants					
Icaraí	122	45	263	2871	
Ilha do Governador	254	48	391	4328	
Pavuna	346	27	288	3490	
Barra da Tijuca	568	211	473	4672	
Cabo Frio	412	222	673	3659	

Table 5. Mean	illicit drug	consumption rates
Lable 5. Mican	mich urug	consumption rates

Abbreviations: WWTP - Wastewater Treatment Plant; AMP – amphetamine; MDMA – 3,4methylenedioxymethamphetamine; COC – cocaine; THC-COOH – 11-nor-9-carboxy- Δ^9 -tetrahydrocannabinol;

(<) below LOQ.

The highest estimated illicit drug consumption rate was obtained for marijuana (4672 mg/1000 p/day (15-64 years)), followed by cocaine (673 mg/1000 p/day (15-64 years)), amphetamine (568 mg/1000 p/ day (15-64 years)), and ecstasy (222 mg/1000 p/day (15-64 years)).

The data found for marijuana are significantly close to other studies, such as those reported in some European cities, for example Turkey (3577 mg/day/1000 inhabitants) ³⁰, and Zagreb/Croatia (5214 mg/day/1,000 inhabitants) ²⁶. For cocaine consumption rate is like reported for Barcelona/Spain (965 mg/1000 p/day (15-64 years)) ¹¹. For amphetamine consumption rate the result are slightly smaller than the found by Zuccato et al. ³¹ in London (690 mg/day/1,000 inhabitants). For ecstasy consumption rate the result is slightly bigger than the found by Daglioglu et al. ³⁰ in Turkey (130 mg/day/1,000 inhabitants).

IV. Discussion

Cannabis was the most used illicit drug we tested, followed by cocaine, amphetamine and MDMA. Our results indicate significant (and worrying) drug use in the regions surveyed, comparable with data found in major global centers. Furthermore, important differences in drug use are attributable to suburbs, but the findings are more complex when neighborhoods are considered, and population density and disadvantage are controlled for. At the individual level, residents of advantaged neighborhoods are more aware of drug sales but are more likely to be users, and there is no relationship between social class and drug dependence. Regarding drug policy, those who have focused attention on poor, largely urban areas have assumed that residents of such neighborhoods (disproportionately members of racial minorities) have substantially higher rates of illicit drug use than the general population. The present study provides contrasting evidence that substance use among residents of these communities varies relatively little compared with the observable harms associated with drug sales.

In the past, methods of measuring drug use in society have relied on community and government surveys. Surveys are often open to self-report bias, as they rely on an individual's recollection of events. This problem can be compounded when examining the prevalence of illicit drug use, as the physiological and psychological effects of drugs can further impact recall. For example, the effects of cannabis use include polyphagia, colloquially known as the "munchies", euphoria and impaired short-term memory; or cocaine use causes paranoia, mydriasis and extreme euphoria and energy. It is recognised in law that the actions and memory of an individual under the influence would often result in their statement being discredited in court. To this end, then, the reliability of the individual's recall of events of drug use becomes further unreliable ³².

Illicit drug use has become an epidemic in many societies, placing burdens on health, society, law enforcement, and government. Numerous scientific studies focused on illicit drug use have found that cocaine, methamphetamine, amphetamine, ecstasy, and marijuana, to name a few, are typically the drugs with the highest rates of abuse ³³. An emerging class of drugs of abuse are New Psychoactive Substance (NPS), which

are designed and created to mimic the physiological and psychological effects of existing psychoactive drugs. These are particularly significant because many are not covered by current legislation, making them technically "legal" for use³⁴.

Although drug use may have gradually increased over the years, there has been an emergence of more potent and dangerous drugs ³⁵. New synthetic psychoactive drugs are an emerging group of drugs that are entering circulation. As technology advances, new synthetic drugs enter the scene, requiring improved screening techniques to accurately assess their contribution to community drug use. Typically, basic screening methods only look for chemicals that have been specifically targeted. Newer screening methods aim to identify new substances without deliberately targeting specific ones ³⁶. With more developed and refined techniques, the improvement and spread of WBE use could potentially identify trends in drug use that could then be used to design programs or campaigns to combat better the use of dangerous illicit drugs that harm the community ³.

WBE has been increasingly used as an additional source of information on the consumption of illicit drugs^{25,26,31}. The main advantage of this innovative approach is its objectivity, which is based on highly accurate chemical measurements of selected drug biomarkers in wastewater, and its suitability for near-real-time tracking of the changes in drug consumption patterns within the selected communities. Wastewater analysis can provide information about spatial and temporal variations of illicit drugs use as well as on the impact of special events such as national holidays or music festivals on drug consumption patterns ³¹. The first multi-approach studies recommend that wastewater analysis can predict results from population surveys. Closer relationship between epidemiologists and legal authorities will expand the perception of the right drug situation and permit for a better evaluation of interventions ³⁷.

However, there are still many challenges and opportunities in using WBE to detect drugs in sewage, such as: (i) The stability of biomarkers in wastewater, especially in natural environments, still needs to be further studied; (ii) The analytical method needs to be continuously improved. The chromatography-mass spectrometry method is a complex, expensive and time-consuming operation, but it has broad prospects in screening NPS and unknown metabolites. Optical and electrochemical analysis is the development direction of future illicit drug detection in wastewater. However, further studies are needed to determine the aspects of stability, accuracy, and large-scale application. (iii) It is necessary to establish relevant evaluation models for the study of error and uncertainty. How to extract more information from existing test results to support the prevention and control of illicit drugs is also a promising direction that deserves focus ³⁸. Although mass spectrometry faces some technical, privacy and ethical challenges, it still has enormous potential. In the future, we can expect a broader application of WBE in the field of drug abuse and public health and hope that this method can be improved and developed to provide data support that tracks the increase in use and types of illicit drugs consumed.

V. Conclusion

The data confirm the pervasiveness of methamphetamine in the surveyed area and support its continued prioritization in public health and enforcement policy. There were intraregional differences in drug use. Use of cannabis, cocaine, amphetamine, and MDMA was higher in higher-income cities, highlighting the importance of location-specific supply dynamics and local consumer preferences; however, lower-income and densely populated neighborhoods also had significant use.

The data show that use occurs habitually and recreationally. These patterns, however, cannot be explained solely by differences in urbanization or population size. In the region studied, it is clear that drug trafficking occurs systematically and the amount consumed is striking, since the levels are either equal to or higher than those in developed regions of the world, despite the fact that we are located in a third world country, with a highly polarized income distribution, with the majority of the population belonging to the middle or lower social class. Furthermore, the country lacks incentives for drug research, since with increasingly smaller investments and no focus on research, the data on the problem of drug use and consumption, as specifically explained here, do not have the desired dispersion of systematic monitoring, which does not demonstrate the worrying reality in which we are immersed.

Finally, the research shows that WBE provides valuable insights into the spatial, temporal, and socioeconomic patterns of drug use and, with complementary information, can help guide the development of nested drug policies at local, regional, and national scales in response to the findings.

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Conflicts of interest The authors declare no conflicts of interest.

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